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1	1248	(514/456).CCLS.	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:26
2	1658	(514/456).CCLS.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/11/04 14:38
3	60520	tea	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:38
4	106	((514/456).CCLS.) and tea	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:40
5	76044	hyperlipidemia lipid	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:41
6	41	((514/456).CCLS.) and tea) and (hyperlipidemia lipid)	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:56
7	2	("2004097432").PN.	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:58
8	1	("20040097432").PN.	USPAT; EPO; JPO; DERWENT; USOCR	2004/11/04 14:58

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*** YOU HAVE NEW MAIL ***

=> s theaflavin?

L1 654 THEAFLAVIN?

=> s (lipid? or cholesterol or hyperlipidemia)

320049 LIPID?

149564 CHOLESTEROL

8858 HYPERLIPIDEMIA

L2 410046 (LIPID? OR CHOLESTEROL OR HYPERLIPIDEMIA)

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L3 16 L1 (12A) L2

=> s l1 (12w) l2

L4 12 L1 (12W) L2

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L3 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

2004:414608 Document No. 140:400086 **Theaflavins** for the treatment of **hyperlipidemia** and/or hypercholesterolemia. Roh-Schmidt, Haeri; Roufs, James B. (Access Business Group International LLC, USA). U.S. Pat. Appl. Publ. US 2004097432 A1 20040520, 7 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-700222 20031103. PRIORITY: US 2002-PV423612 20021104.

AB A method of treating elevated cholesterol levels, **hyperlipidemia** and/or hypercholesterolemia in a mammal includes administering an effective amount of **theaflavins**, thearubigins, and their mixts. The theaflavins include theaflavin and gallate esters of theaflavin, particularly those obtained from tea. The gallate esters include theaflavin-3-gallate, theaflavin-3'-gallate, and theaflavin-3,3'-digallate.

=> d 2-16 cbib abs

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2004:414607 Document No. 140:412294 Compositions of theaflavins for dietary supplement. Zhao, Jian; Zhou, Rui; Chen, Hu; Vaughn, Thomas M. (USA). U.S. Pat. Appl. Publ. US 2004097430 A1 20040520, 17 pp., Cont.-in-part of U.S. Ser. No. 306,204, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2003-601314 20030620. PRIORITY: US 2001-PV333515 20011128; CN 2002-111512 20020426; US 2002-PV413576 20020924; US 2002-306204 20021127.

AB The present invention discloses methods of making theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3'-digallate

and their mixture, pharmaceutical compns. comprising the theaflavins or their mixture, dietary supplement compns. of theaflavins or their mixts., and methods for using either the mixture of theaflavins or individual theaflavins to treat or prevent various diseases. For example, green tea leaves (100 kg) and 0.15 M phosphate buffer (1000 L, pH 6.4) were fermented at 30° for about 1 h under a 22% oxygen atmospheric. The reaction mixture was centrifuged, and the supernatant was decanted and filtered. About 1000 L of Et acetate was added to the aqueous filtrate to terminate fermentation, the organic layer was washed with 5% NaHCO₃, and Et acetate

was removed in vacuo. The residue was dissolved in 40% Et acetate/hexane, loaded onto a silica gel column, and eluted with 40% Et acetate/hexane to provide a mixture of theaflavins. The mixture comprised 46.8% theaflavin, 18.5% theaflavin-3-gallate, 13.7% theaflavin-3'-gallate and 20.3% theaflavin-3,3'-digallate. Choleve, the mixture of **theaflavins** obtained, was administered orally to patients with mild to moderate **hyperlipidemia** for 12 wk. After 12 wk, serum total cholesterol and LDL-cholesterol decreased by 11.3% and 16.4%, resp., indicating the potential of Choleve in treating and preventing coronary heart disease. No adverse reactions to Choleve occurred during this clin. trial.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2004:328306 Document No. 141:88136 Antioxidant activity of tea theaflavins and methylated catechins in canola oil. Su, Ya-Lun; Xu, Jin-Ze; Ng, Chi Ho; Leung, Lai Kwok; Huang, Yu; Chen, Zhen-Yu (Food and Nutritional Science Programme, Department of Biochemistry, The Chinese University of Hong Kong, Hong Kong, Peop. Rep. China). Journal of the American Oil Chemists' Society, 81(3), 269-274 (English) 2004. CODEN: JAOCA7. ISSN: 0003-021X. Publisher: AOCs Press.

AB The present study examined the antioxidant activity of black tea theaflavins and catechin derivs. in canola oil. Oxidation was conducted at 95° by monitoring the oxygen consumption and decreases in the linoleic and α -linolenic acids of canola oil. All were tested at a concentration of 0.5 mM. Catechins, including (-)-epicatechin, (-)-epicatechin gallate, (-)-epigallocatechin, and (-)-epigallocatechin gallate (EGCG), were more effective than theaflavins, namely, theaflavin-1, theaflavin-3-gallate, **theaflavin-3'-gallate**, and **theaflavin-3,3'-digallate** (TF3), against the **lipid** oxidation of canola oil. Among the four theaflavins, TF3 was the most effective, whereas among the four catechins, EGCG was the most potent. Under the same conditions, all theaflavins and catechins were more powerful than BHT as an antioxidant in heated canola oil. Little or no difference in antioxidant activity was observed between each catechin and epimer pair. Methylation of the 3'-OH led to a significant loss of antioxidant activity of the catechins.

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2003:565076 Document No. 139:207512 Cholesterol-lowering effect of a theaflavin-enriched green tea extract: a randomized controlled trial. Maron, David J.; Lu, Guo Ping; Cai, Nai Sheng; Wu, Zong Gui; Li, Yue Hua; Chen, Hui; Zhu, Jian Qiu; Jin, Xue Juan; Wouters, Bert C.; Zhao, Jian (Division of Cardiovascular Medicine, Vanderbilt University Medical Center, Nashville, TN, USA). Archives of Internal Medicine, 163(12), 1448-1453 (English) 2003. CODEN: AIMDAP. ISSN: 0003-9926. Publisher: American Medical Association.

AB Tea consumption has been associated with decreased cardiovascular risk, but potential mechanisms of benefit are ill-defined. While epidemiol. studies suggest that drinking multiple cups of tea per day lowers low-d. lipoprotein cholesterol (LDL-C), previous trials of tea drinking and administration of green tea extract have failed to show any impact on lipids and lipoproteins in humans. Our objective was to study the impact of a **theaflavin-enriched green tea extract on the lipids** and lipoproteins of subjects with mild to moderate hypercholesterolemia. The double-blind, randomized, placebo-controlled, parallel-group trial was set in outpatient clinics in 6 urban hospitals in China. A total of 240 men and women 18 yr or older on a low-fat diet with mild to moderate

hypercholesterolemia were randomly assigned to receive a daily capsule containing theaflavin-enriched green tea extract (375 mg) or placebo for 12 wk. Main outcome measures were mean percentage changes in total cholesterol, LDL-C, high-d. lipoprotein cholesterol (HDL-C), and triglyceride levels compared with baseline. After 12 wk, the mean \pm SEM changes from baseline in total cholesterol, LDL-C, HDL-C, and triglyceride levels were $-11.3\% \pm 0.9\%$ ($P=.01$), $-16.4\% \pm 1.1\%$ ($P=.01$), $2.3\% \pm 2.1\%$ ($P=.27$), and $2.6\% \pm 3.5\%$ ($P=.47$), resp., in the tea extract group. The mean levels of total cholesterol, LDL-C, HDL-C, and triglycerides did not change significantly in the placebo group. No significant adverse events were observed. The theaflavin-enriched green tea extract we studied is an effective adjunct to a low-saturated-fat diet to reduce LDL-C in hypercholesterolemic adults and is well tolerated.

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2003:390527 Document No. 139:116750 Antioxidative activities of black tea theaflavins in the presence of ascorbic acid and ferrous and ferric ions under autoxidative and photosensitized oxidation conditions. Yoshioka, Masako; Sato, Miki; Tezuka, Yuko (Department of Food and Nutrition Sciences, Miyagi Gakuin Women's College, Sendai, Miyagi, 981-8557, Japan). Seikatsu Kankyo Kagaku Kenkyusho Kenkyu Hokoku (Miyagi Gakuin Joshi Daigaku), 35, 1-6 (English) 2003. CODEN: SKKKGG. ISSN: 1346-6534. Publisher: Miyagi Gakuin Joshi Daigaku Seikatsu Kankyo Kagaku Kenkyusho.

AB Theaflavins (theaflavin A(TA) and theaflavin B(TB)) and epigallocatechin gallate (EGCG) were prepared from black and green tea, resp. Antioxidative potencies of the tea polyphenols, BHT and α -tocopherol were compared in the presence of a water-soluble antioxidant, ascorbic acid, and lipid-oxidation accelerators, Fe^{2+} and Fe^{3+} , under autoxidative and photosensitized oxidative conditions. It was concluded that ascorbic acid worked synergistically as an antioxidant even in oil suspension with such antioxidants as BHT, TA, EGCG, TB and α -tocopherol. Under an autoxidative condition in the presence of ascorbic acid, BHT exhibited the most potent antioxidative efficiency followed by TA and EGCG, while TA was found the most potent under photosensitized oxidative condition with ascorbic acid. In the presence of iron ions as a lipid oxidation accelerator, TA was found to be the most effective antioxidant both under autoxidn. and photosensitized oxidation conditions.

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2003:193543 Document No. 138:367880 Evaluation of the anti-oxidative effect (in vitro) of tea polyphenols. Hashimoto, Fumio; Ono, Masateru; Masuoka, Chikako; Ito, Yasuyuki; Sakata, Yusuke; Shimizu, Keiichi; Nonaka, Gen-Ichiro; Nishioka, Itsuo; Nohara, Toshihiro (Faculty of Agriculture, Kagoshima University, Korimoto 1-21-24, Kagoshima, 890-0065, Japan). Bioscience, Biotechnology, and Biochemistry, 67(2), 396-401 (English) 2003. CODEN: BBBIEJ. ISSN: 0916-8451. Publisher: Japan Society for Bioscience, Biotechnology, and Agrochemistry.

AB Forty-three polyphenols from tea leaves were evaluated for their anti-oxidative effect against lipid peroxidn. by the ferric thiocyanate method in vitro. Among these, 1,4,6-tri-O-galloyl- β -D-glucose (hydrolyzable tannin) showed the highest anti-oxidative activity against lipid peroxidn., even stronger than that of 3-tert.-butyl-4-hydroxyanisole (BHA). The assay demonstrates that tea polyphenols, except for desgalloylated dimeric proanthocyanidins that possess a catechin structure in the upper unit and desgalloylated flavan-3-ols, and excepting theaflavin 3,3'-di-O-gallate, had more anti-oxidative activity than that of α -tocopherol. The chemical structure-activity relationship shows that the anti-oxidative action advanced with the condensation of two mols. of flavan-3-ols as well as with 3-O-acylation in the flavan skeleton such as that by galloyl, (3'-O-methyl)-galloyl, and p-coumaroyl groups.

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

2000:466100 Document No. 133:329192 Black tea **theaflavins** are potent inhibitors of squalene epoxidase, a key enzyme in **cholesterol** biosynthesis. Abe, Ikuro; Seki, Takahiro; Noguchi,

Hiroshi; Hara, Yukihiro (School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, Japan). Nippon Shokuhin Kagaku Gakkaishi, 7(1), 47-50 (English) 2000. CODEN: NSKGF4. ISSN: 1341-2094. Publisher: Nippon Shokuhin Kagaku Gakkai.

- AB Squalene epoxidase (SE) is a non-metallic flavoprotein monooxygenase that catalyzes the conversion of squalene to 2,3-oxidosqualene, a rate-limiting step of cholesterol biosynthesis. A study was conducted which shows that theaflavins, the major component of black tea polyphenols, are excellent inhibitors of SE. In the fermentation process of tea leaves, the monomeric flavan-3-ols undergo extensive enzymic oxidation leading to the formation of bis-flavanols; theaflavins, and other catechin oligomers. As in the case of green tea polyphenols, theaflavins have been also shown to have a variety of biol. activities including cancer prevention as well as induction of apoptosis.

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

1997:680393 Document No. 127:355154 Influence of **theaflavin** on blood **lipid** and Hemorrheologic parameters. Meng, Mei; Sun, Aihua (Guangzhou Hongshizhui Hospital, Canton, 510220, Peop. Rep. China). Guangdong Yixue, 18(6), 421 (Chinese) 1997. CODEN: GUYIEG. ISSN: 1001-9448. Publisher: Guangdongsheng Yixue Qingbao Yanjiusuo.

- AB 50 Inpatients with 43 hypertensives (31 cases complicated with coronary disease), 4 diabetics and 3 cerebral infarctions received addnl. 250 mg theaflavin, an active ingredient extracted from tea, t.i.d. for 2 mo. Half of the patients had significant decreased blood total cholesterol and triglycerides, and most of their blood rheol. parameters improved significantly. The results suggest that theaflavin is effective in management of cardiovascular disease.

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

1997:498140 Document No. 127:148439 Antioxidants in tea and their physiological functions. Hara, Yukihiro (Food Research Labs, Mitsui Norin Co., Ltd., Fujieda City, 426, Japan). Food and Free Radicals, [Proceedings of the Symposium on Food and Free Radicals], 1st, Yamagata, Japan, June 16, 1994, Meeting Date 1994, 49-65. Editor(s): Hiramatsu, Midori; Yoshikawa, Toshikazu; Inoue, Masayasu. Plenum: New York, N. Y. (English) 1997. CODEN: 64TPA6.

- AB A review with 10 refs. on the author's work on antioxidants in tea. Topics discussed include: method of extracting tea polyphenols, radical-scavenging action of tea catechins, antioxidative action of tea catechins in edible fats and oils, antioxidative action of **theaflavins** on erythrocyte membrane **lipids**, influence of catechin feeding on the levels of α -tocopherol, TBARS in plasma and erythrocyte, and effects of long-term dietary supplementation of tea polyphenols on lipid peroxide levels in rats.

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

1994:603678 Document No. 121:203678 Protective role of phenolic antioxidants in dietary plants against oxidative damage. Osawa, T.; Katsuzuki, H.; Kumon, H.; Kawakishi, S.; Yamashita, K.; Nakayama, T.; Hara, Y. (Dep. Appl. Biol. Sci., Nagoya Univ., Nagoya, Japan). International Congress Series, 1058(Frontiers of Reactive Oxygen Species in Biology and Medicine), 333-6 (English) 1994. CODEN: EXMDA4. ISSN: 0531-5131.

- AB Sesaminol from sesame seeds was effective as a lipid-soluble antioxidant against lipid peroxidn., but did not have a direct protective effect on DNA oxidative damage. Catechins and **theaflavins** from green and black teas were effective antioxidants for **lipid** peroxidn. and DNA oxidative damage, and the gallic acid moiety of theaflavins is considered essential for their antioxidant activity.

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

1994:261302 Document No. 120:261302 Antioxidative effects of black tea **theaflavins** and thearubigin on **lipid** peroxidation of rat liver homogenates induced by tert-butyl hydroperoxide. Yoshino, Kyoji; Hara, Yukihiro; Sano, Mitsuaki; Tomita, Isao (Dep. Chem. Biochem., Numazu

Coll. Technol., Numazu, 410, Japan). Biological & Pharmaceutical Bulletin, 17(1), 146-9 (English) 1994. CODEN: BPBLEO. ISSN: 0918-6158.

AB The antioxidative activity of theaflavins (TFs) and thearubigin (TR) purified from the infusion of black tea leaves was examined using the tert-Bu hydroperoxide-induced lipid peroxidn. of rat liver homogenates. The concns. which produced 50% inhibition of lipid peroxidn. (IC50) by theaflavin (TF), theaflavin monogallate-A (TFM-A), and TR were 4.88×10^{-4} , 4.09×10^{-4} , and $4.95 \times 10^{-4}\%$ (w/v), resp. The antioxidative activity of these compds. was higher than that of glutathione, L(+)-ascorbic acid, dL- α -tocopherol, butylated hydroxytoluene, Bu hydroxyanisole, etc., but was lower than the activity of (-)-epicatechin gallate, (-)-epigallocatechin, and (-)-epigallocatechin gallate. As to the IC50 in molarity, the antioxidative activity of TFM-A was the second highest among all the samples used in this study. The antioxidative activity of lyophilized tea infusions was compared. The activity of black tea was about as potent as that of green tea. These results suggest that black tea infusion containing TFs and TR could inhibit lipid peroxidn. in biol. conditions in the same way as green tea infusion containing epicatechins.

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
1994:185151 Document No. 120:185151 Antioxidative and antimutagenic effects of theaflavins from black tea. Shiraki, Mayumi; Hara, Yukihiko; Osawa, Toshihiko; Kumon, Harue; Nakayama, Tsutomu; Kawakishi, Shunro (Food Res. Lab., Mitsui Norin Co., Ltd., Fuijieda, 426, Japan). Mutation Research, 323(1-2), 29-34 (English) 1994. CODEN: MUREAV. ISSN: 0027-5107.

AB **Theaflavins** polyphenolic ingredients of black tea, were observed to inhibit in vitro lipid peroxidn. in the erythrocyte membrane ghost and microsomal systems. Theaflavins also showed inhibition of DNA single-strand cleavage and mutagenicity, both induced by hydrogen peroxide. These results suggest that theaflavins scavenge radicals to produce antioxidative and antimutagenic effects. It was also found that the gallic acid moiety of theaflavins is essential for their potent antioxidative activities.

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